

In re: Foster et al.
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REMARKS

Claims 1-17 are pending in this application. Claims 1, 3, 7, 11-16 are amended herein in order to further clarify the invention. Support for these amendments is found throughout the originally filed specification and claims, as set forth below. Claims 2, 4-6, 8-10 and 17 are canceled herein without prejudice. Applicants respectfully request entry of the amendments above and hereby request further consideration of the application in view of the amendments and the following remarks.

I. Objection to the Disclosure.

The Office Action states that the disclosure is objected to because it does not include subheadings. Office Action, page 3.

The specification is amended herein to include subheadings as requested. Accordingly, Applicants respectfully submit that the objection is overcome and respectfully request its withdrawal.

II. Claim Rejection under 35 U.S.C. § 112.

Claim 16 stands rejected under 35 U.S.C. § 112 as allegedly being indefinite. Office Action, page 3. The Office Action states that it is unclear what one would consider as a further concentrated salt wash. *Id.*

Claim 16 is amended herein to recite the method according to Claim 1, comprising washing the substrate in a further step with the concentrated sodium chloride salt solution. Support for this amendment can be found throughout the specification and claims as originally filed, for example, claim 9. Thus, Applicants respectfully submit that claim 16 is clarified and respectfully request the withdrawal of this rejection.

III. Claim Rejections under 35 U.S.C. § 102 (a).

Claims 1-8, and 10-11 stand rejected under 35 U.S.C. § 102(a) as being anticipated by Prusiner (WO01/54736A2). The Office Action states that Prusiner teaches cleaning substrates in order to remove prions by washing with a salt solution with concentration ranges between 0.01-10.0 % by weight of protein denaturant. Office Action, pages 3-4.

As presented herein, Claim 1 recites a method of cleaning a substrate of chromatographic materials in order to remove adsorbed prion infectivity, comprising washing the substrate with a concentrated sodium chloride salt solution, wherein the salt solution comprises a concentration of at least 1.0M. Support for these amendments is found in original claims 2 and 9. Prusiner does not teach the use of a sodium chloride solution for cleaning a substrate of chromatographic materials in order to remove adsorbed prion infectivity as is recited in pending claim 1. Thus, Applicants submit that pending claim 1, and claims dependent thereon, are novel over Prusiner and respectfully request withdrawal of this rejection.

IV. Claim Rejections under 35 U.S.C. § 102 (e).

Claims 1, 4-8, and 16-17 stand rejected under 35 U.S.C. § 102(e) as being anticipated by McDonnell et al. (U.S. Application Publication No. 2003/0086820). The Office Action states that McDonnell et al. teaches a method of cleaning a surface to remove infective prions by treating with an alkaline cleaning solution and that the alkaline solution comprises EDTA salts having a concentration of about 1-15% by weight. Office Action, page 4.

As stated above, claim 1 recites a method of cleaning a substrate of chromatographic materials in order to remove adsorbed prion infectivity, comprising washing the substrate with a concentrated sodium chloride salt solution, wherein the salt solution comprises a concentration of at least 1.0M. McDonnell et al. discusses the use of EDTA salts as a chelating agent for addressing water hardness salts that become deposited on the equipment to be cleaned. McDonnell et al. does not disclose

the use of a sodium chloride solution for cleaning a substrate of chromatographic materials in order to remove adsorbed prion infectivity as is recited in the pending claims. Thus, Applicants submit that the pending claims are novel over McDonnell et al. and respectfully request withdrawal of this rejection.

V. Claim Rejections under 35 U.S.C. § 102 (b).

Claim 17 stands rejected under 35 U.S.C. § 102 (b) as being anticipated by Gawryl et al. (U.S. Patent No. 5808011). The Office Action states that Gawryl et al. teaches a 1.0M NaCl solution for removal of prions from a chromatographic column. Office Action, page 5. Applicants respectfully disagree with this characterization of Gawryl et al.

As an initial point, the Office Action fails to cite to a specific recitation in Gawryl et al. where a 1.0M NaCl solution is discussed for removal of prions from a chromatographic column. Applicants can only surmise that the Office Action is referring to column 4, lines 27-31, wherein a "buffer four" is discussed. This buffer is described as a NaCl/Tris solution with a NaCl concentration about 1.0M. However, nowhere in Gawryl et al. is this buffer, or any other NaCl buffer or solution, used for removal of prions from a chromatographic column.

Garwyl et al. in column 7, lines 47-61, discusses the elution of prions from an anion exchange column using only buffers one, two and three (the buffers are described in column 4, lines 27-31). The infectivity data presented in the Table in columns 9 and 10 clearly show that the prions are removed from the column by the second buffer. The second buffer is a Tris buffer; it is not a NaCl buffer or solution. Furthermore, the NaCl buffer, which is mentioned but not used in Garwyl, comprises 1.0M NaCl, in contrast to the present invention, which teaches a concentration of at least 1.0M NaCl. Thus, Gawryl et al. fails to describe a method of cleaning a substrate of chromatographic materials in order to remove adsorbed prion infectivity, comprising washing the substrate with a concentrated sodium chloride salt solution, wherein the salt solution comprises a concentration of at least 1.0M as is recited in the

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pending claims. However, Applicants have canceled claim 17, thus this rejection is obviated and applicants respectfully request its withdrawal.

VI. Claim Rejections under 35 U.S.C. § 103.

A. Rejection of claims 12-15 under 35 U.S.C. § 103

Claims 12-15 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over McDonnell et al. (U.S. Patent No. 5808011). The Office Action states that McDonnell et al. teaches a one step process of using the salt solution in combination with the alkali and that it would have been within the level of the skilled artisan to modify the method of McDonnell et al. to include multiple cleaning steps using salt and alkaline solutions. Office Action, page 6.

As discussed above, claim 1 recites a method of cleaning a substrate of chromatographic material in order to remove adsorbed prion infectivity, comprising washing the substrate with a concentrated sodium chloride salt solution, wherein the salt solution comprises a concentration of at least 1.0M. Applicants respectfully submit that the only salts discussed in McDonnell et al. include chelating agents such as EDTA (paragraph 0038), surfactants such as those listed in paragraph 0039, and anti-redeposition agents such as those listed in paragraph 42. None of the salts discussed in McDonnell et al. includes or suggests NaCl. Further, McDonnell et al. fails to disclose or suggest the washing of chromatographic materials in order to remove adsorbed prions as is recited in the pending claims. Thus, McDonnell et al. does not disclose all of the elements of claim 1 of the present invention. Claims 12-15 depend from claim 1. Thus, McDonnell et al. does not recite all of the elements of claims 12-15. Accordingly, Applicants respectfully submit that claims 12-15 are patentable over McDonnell et al. and respectfully request that this rejection be withdrawn.

B. Rejection of claims 1-3, 6-9, and 11-16 under 35 U.S.C. § 103

Claims 1-3, 6-9, and 11-17 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Uhlen et al. (U.S. Patent No. 831161) in view of Gawryl et al. (U.S. Patent No. 5808011). The Office Action states that Uhlen et al. teaches cleaning and sanitizing chromatographic columns by washing with 0.1 to 1.0M NaOH in combination with NaCl for removing prions. Office Action, page 6. The Office Action further states that Gawryl et al. teaches a method for removing prions from chromatographic columns using buffers such as 1.0M NaCl to elute the prion from the column. *Id.* The Office Action concludes that it would have been obvious to a skilled artisan to modify the method of Uhlen et al. to include 1.0M NaCl as taught by Gawryl et al., for the purposes of eluting prions from the column. Applicants respectfully disagree.

The statement in Uhlen et al. that is cited in the Office Action specifically recites "[t]he recognized standard for cleaning and sanitizing separation media and systems is NaOH, often in combination with NaCl. An applied 0.1-1.0M NaOH solution is able to remove viruses, bacteria, nucleic acid, proteins, yeasts, endotoxins, prions and other contaminating agents." (*see* column 2, lines 9-13). Applicants respectfully submit that this recitation is simply a generalized statement about the state of the art regarding the use of NaOH for removing contaminating agents chromatography materials wherein sometimes NaCl is included. Nowhere in Uhlen et al. is it taught or suggested that NaCl could be used alone for the purpose of removing prions from chromatographic materials as is disclosed in claim 1 of the present invention. Further, there is no suggestion or teaching in the prior art such that one of ordinary skill in the art would have been motivated to modify Uhlen et al. or to combine it with Gawryl et al. to achieve a method of cleaning a substrate of chromatographic materials in order to remove adsorbed prion infectivity, comprising washing the substrate with a concentrated sodium chloride salt solution, wherein the salt solution comprises a concentration of at least 1.0M as is recited in the pending claims. Thus, Uhlen et al. fails to teach or suggest the subject matter of claims 1-3, 6-

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9, and 11-17. Furthermore, Gawryl et al. fails to remedy the deficiencies of Uhlen et al.

As discussed previously in this response, Gawryl et al. does not disclose the use of any NaCl solution or buffer for washing of prions from any substrate including chromatographic materials. The 1.0M NaCl buffer mentioned in Gawryl et al. is never used in any procedures, including those focused on removing prions from substrates. A careful reading of Gawryl et al. shows that buffers one, two and three are used in eluting prions from the anion exchange material and that it is buffer two (a Tris buffer) that removes the prions (*see* column 7, lines 47-61; Table, columns 9 and 10). Thus, Gawryl et al. does not teach or suggest the use of any NaCl solution, much less a 1.0M NaCl solution, for the removal of prions from chromatographic materials as is recited in the pending claims. Therefore, Uhlen et al. and Gawryl et al. fail to teach or suggest the subject matter of the pending claims. Accordingly, Applicants respectfully submit that claims 1-3, 6-9, and 11-17 are nonobvious over Uhlen et al. in view of Garwyl et al. and respectfully request that this rejection be withdrawn.

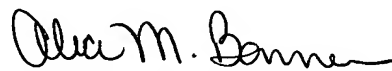
Finally, with regard to the statement in the Office Action on page 7 that "it would have been well within the level of the skilled artisan to determine what concentration levels of NaCl solution are needed in order to elute the prions from the chromatographic column," Applicants respectfully disagree. As stated in the present application, the inventors themselves were surprised that prion infectivity appeared to follow conventional ion exchange behavior with an anion exchange matrix and that they could elute the prions using high salt concentrations (present application, page 4, paragraphs 1 and 4). This was such a surprise that, in their initial experimental protocol, the inventors did not optimize for measuring prion infectivity levels eluted with the salt washed. *Id.* Accordingly, it would not have been within the level of the one of ordinary skill at the time the present application was filed to determine what concentration levels of NaCl would be needed in order to elute prions from chromatographic materials.

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In view of the foregoing, Applicants believe that the points and concerns raised by the Examiner in the Action have been addressed in full, it is respectfully submitted that this application is in condition for allowance. Should the Examiner have any remaining concerns, it is respectfully requested that the Examiner contact the undersigned Attorney at (919) 854-1400 to expedite the prosecution of this application to allowance.

No fee is believed due. However, the Commissioner is hereby authorized to charge any deficiency or credit any refund to Deposit Account No. 50-0220.

Respectfully submitted,



Alice M. Bonnen
Registration No. 57,154


Myers Bigel Sibley & Sajovec, P.A.
P. O. Box 37428
Raleigh, North Carolina 27627
Telephone: (919) 854-1400
Facsimile: (919) 854-1401
Customer No. 20792

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Amelia Tauchen